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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/126,096	07/30/1998	EUGENE D. THORSETT	002010-137	8518

21839 7590 05/23/2003

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EXAMINER

RAO, DEEPAK R

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory ActionApplication No.
09/126,096Applicant(s)
Thorsett et al.Examiner
Deepak RaoArt Unit
1624

— The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

THE REPLY FILED May 5, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on May 5, 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE:

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
see attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: _____

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s): _____.

10. ☐ Other: _____

DEEPAK RAO
PRIMARY EXAMINER
ART UNIT 1624

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ADVISORY ACTION

The request for reconsideration has been entered and considered but does not overcome the rejection because there is nothing on to establish that the claimed compounds have unexpected properties when compared to the reference compounds. As explained in the previous office actions, the instant compounds differ from the reference compounds by having the R⁴ substituent (e.g., CH₃) on the carbon adjacent to the nitrogen atom, as compared to the reference compounds wherein the carbon is unsubstituted (i.e., substituted with H). The reference compounds are taught to be useful as therapeutic agents for treatment of diseases mediated by VLA-4, which provides sufficient motivation to one of ordinary skill in the art to prepare the homologs with the expectation of obtaining compounds having similar properties. Applicant has not provided any explanation or data refuting that the homolog would not have the properties of the reference disclosed unsubstituted compound.

Applicant submits that the claimed compounds and the reference compounds do not have the same properties, however, no explanation or data is provided to show the indicated difference in properties. Applicant relies on the reference Salgado et al., to rebut the prima facie case of obviousness, arguing that the reference shows superior properties for α,α -disubstituted compounds, however, the reference compounds are 2,2-dialkylcyclopropane carboxylic acids as compared to the instantly claimed nitrogen heterocycles, e.g., pyrrolidine. First, the reference statement regarding the enhanced property of the α,α -disubstituted compound was not stated in comparison of the α,α -disubstituted compound with the α -(mono)substituted compound.

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According to Salgado, 1-amino-2-substituted-cyclopropane-1-carboxylic acids are also effective and useful as plant growth regulators. Further, it is well established that cyclopropane itself is a rigid molecule and shows chemical properties that are entirely different from other molecules including many of the members of cycloalkane family. This very rigidity of the cyclopropane may be contributing to the conformational restrictions discussed in the reference. Therefore, applicant's arguments in view of Salgado are not sufficient to establish any unexpected properties for the claimed compounds.

Applicant draws attention to the language in *Lalu* - "The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compounds", which has already been established in the present situation. The reference disclosed compounds "as a whole" provide sufficient motivation to one of ordinary skill in the art to prepare the structural homologs thereof by introducing a methyl group in place of the hydrogen, with the reasonable expectation of obtaining compounds having similar properties.

For all the above reasons, the obviousness-type double patenting rejection is maintained.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Deepak Rao
Primary Examiner
Art Unit 1624

May 21, 2003